

CLAIMS

We claim:

1. An isolated substantially homogeneous *mpl* ligand polypeptide.
2. An isolated substantially homogeneous *mpl* ligand characterized in that:
 - (1) the ligand stimulates the incorporation of labeled nucleotides (³H-thymidine) into the DNA of IL-3 dependent Ba/F3 cells transfected with human *mpl* P;
 - (2) the ligand is stable to pH 2.5, SDS at 0.1%, and 2M urea;
 - (3) the ligand is a glycoprotein; and
 - (4) the amino-terminal sequence of the polypeptide is selected from the group

SPAPPACDPRLNKLRRDDHVLHGR (SEQ ID NO: *); and
SPAPPACDLRVLSKLLRRDDHVLHSRL (SEQ ID NO: *).
3. An isolated polypeptide comprising the amino-terminal sequence SPAPPACDLRVLSKLLRRDDHVLHSRL (SEQ ID NO: *).
4. The polypeptide of Claim 3 that is unglycosylated.
5. An isolated substantially homogeneous *mpl* ligand polypeptide sharing at least 80% sequence identity with the polypeptide of Claim 3.
6. An isolated polypeptide encoded by a nucleic acid having a sequence that hybridizes under stringent conditions to the complement of the nucleic acid having a sequence of Figure 7 (SEQ ID NO: *) from about nucleotide 119 to about nucleotide 196.
7. The polypeptide of Claim 6 that is biologically active.
8. A fusion comprising the *mpl* ligand of Claim 2 fused to a heterologous polypeptide.

9. An antibody that is capable of binding the *mpl* ligand polypeptide of Claim 3.
10. A hybridoma cell line producing the antibody of Claim 9.
11. An isolated nucleic acid molecule encoding the *mpl* ligand polypeptide of Claim 3.
12. An isolated nucleic acid molecule encoding the *mpl* ligand polypeptide of Claim 2.
13. An isolated nucleic acid molecule comprising the nucleic acid sequence shown in Figure 7 (SEQ ID NO: *) from about nucleotide 119 to about nucleotide 196.
14. An isolated nucleic acid molecule selected from the group consisting of
 - (a) a cDNA clone comprising the nucleotide sequence of the coding region of the *mpl* ligand gene;
 - (b) a DNA sequence capable of hybridizing under stringent conditions to a clone of (a); and
 - (c) a genetic variant of any of the DNA sequences of (a) and (b) which encodes a polypeptide possessing a biological property of a naturally occurring *mpl* ligand polypeptide.
15. The nucleic acid molecule of Claim 11 which is DNA and comprises a sequence encoding the amino acid sequence SPAPPACDLRVLSKLLRDDHVLHSRL (SEQ ID NO: *).
16. The nucleic acid molecule of Claim 11 further comprising a promoter operably linked to the nucleic acid molecule.
17. An expression vector comprising the nucleic acid sequence of Claim 11 operably linked to control sequences recognized by a host cell transformed with the vector.
18. A host cell transformed with the vector of Claim 17.

Sub B2

Sub A9

Sub B3

- Sub
B4
19. A method of using a nucleic acid molecule encoding the *mpl* ligand polypeptide to effect production of the *mpl* ligand polypeptide comprising culturing the host cell of Claim 18.
 20. The method of Claim 19 wherein the *mpl* ligand polypeptide is recovered from the host cell
 21. The method of Claim 19 wherein the *mpl* ligand polypeptide is recovered from the host cell culture medium.
 22. A method of determining the presence of *mpl* ligand polypeptide, comprising hybridizing DNA encoding the *mpl* ligand polypeptide to a test sample nucleic acid and determining the presence of *mpl* ligand polypeptide DNA.
 23. A method of amplifying a nucleic acid test sample comprising priming a nucleic acid polymerase reaction with nucleic acid encoding a *mpl* ligand polypeptide.
 24. A composition comprising the *mpl* ligand polypeptide of Claim 1 and a pharmaceutically acceptable carrier.
 25. A method for treating a mammal having or at risk for thrombocytopenia comprising administering to a mammal in need of such treatment a therapeutically effective amount of the composition of Claim 24.
 26. The composition of Claim 24 further comprising a therapeutically effective amount of an agent selected from the group consisting of a cytokine, colony stimulating factor, and interleukin
 27. The composition of Claim 26 wherein the agent is selected from LIF, G-CSF, GM-CSF, M-CSF, Epo, IL-1, IL-2, IL-3, IL-5, IL-6, IL-7, IL-8, IL-9 and IL-11.